2.0 NON-TECHNICAL ABSTRACT

The $CD4^+$ T cell is an essential component of the body's immune response, and is the primary target of HIV infection. Virus replication in these cells leads to the progressive loss of $CD4^+$ cells resulting in a severe immunocompromised state in the host and eventually death. The use of medications to prevent HIV replication in infected individuals can temporarily control the infection, but these agents are insufficient for long-term control of infection due to the development of drug resistance by the virus. Recently, novel genes have been identified that when present in a $CD4^+$ cell can inhibit HIV production, a strategy known as intracellular immunization. In the proposed study, $CD4^+$ T cells will be isolated from HIV seropositive patients, genetically modified with selected intracellular immunization genes, grown to large numbers in the laboratory, and reinfused into the patient. This treatment approach is called adoptive: immunotherapy, and has been previously shown in mouse models and recently with cytomegalovirus infection in humans, to be safe and to deliver protective anti-viral immunity to the host. The T cells to be used in this immunotherapy study will be modified by retrovirus-mediated gene transfer to express two different HIV-protective genes and a control gene for comparison to determine if these genes can protect $CD4^+$ T cell immunity in patients. This study will provide information on the safety and antiviral effects of adoptive immunotherapy with $CD4^+$ T cells. Moreover, if these genes are effective in preserving cell survival and function, this approach will be used in future studies of T cells to reconstitute HIV specific immunity.